

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



PCT

(10) International Publication Number
WO 2006/014349 A2

(51) International Patent Classification:
C07K 14/505 (2006.01)

(21) International Application Number:
PCT/US2005/023505

(22) International Filing Date: 1 July 2005 (01.07.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/585,262 2 July 2004 (02.07.2004) US
60/584,951 2 July 2004 (02.07.2004) US

(71) Applicants (for all designated States except US): **THE KENNETH S. WARREN INSTITUTE, INC.** [US/US]; 712 Kitchawan Road, Ossining, NY 10562 (US). **CE- RAMI, Anthony** [US/US]; 58a Heritage Hills Road, Somers, NY 10589 (US). **HAND, Carla, Cerami** [US/US]; 11370 Involute Place, Apt. 100, Raleigh, NC 27617-8518 (US). **XIE, Qiao-wen** [US/US]; 30 Sidehill Lane, Yonkers, NY 10710 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **BRINES, Michael** [US/US]; One Wepawaug Road, Woodbridge, CT 06525 (US).

(74) Agent: **HAMBLE, Frederick, J.**; Warren Pharmaceuticals, Inc., 712 Kitchawan Road, Ossining, NY 10562 (US).

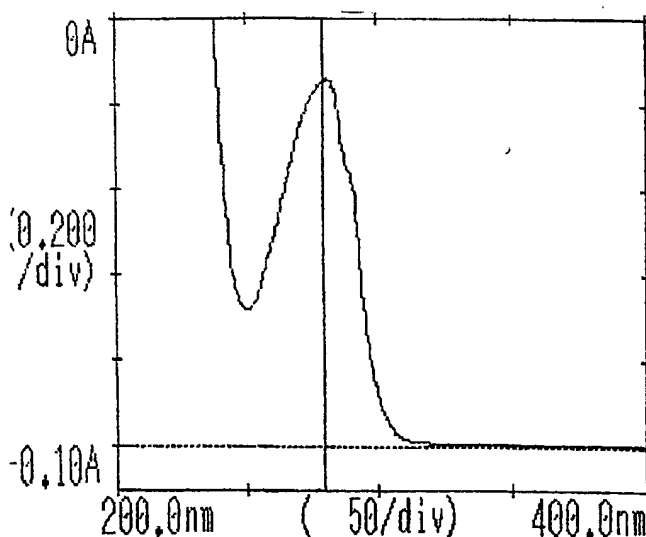
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),

[Continued on next page]

(54) Title: METHOD OF PRODUCING FULLY CARBAMYLATED ERYTHROPOIETIN

Scan of Carbamylated Erythropoietin



(57) Abstract: The present invention relates to a method of carbamylating an erythropoietin such that the resulting carbamylated erythropoietin has less than about 10% free primary amines on the lysines and the N-terminal amino acids, is not digested when exposed to Lys-C proteolysis, exhibits no erythropoietic activity in a TF-1 or UT-7/EPOR cell viability assay at a concentration of 1 µg/ml, and demonstrates a static sciatic index of less than about .65 within a Sciatic Nerve Assay. Additionally, the invention is related to pharmaceutical compositions containing carbamylated erythropoietins of the invention and the use of the pharmaceutical compositions for the treatment of conditions and diseases of excitable tissues.

WO 2006/014349 A2



European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Published:

- without international search report and to be republished upon receipt of that report